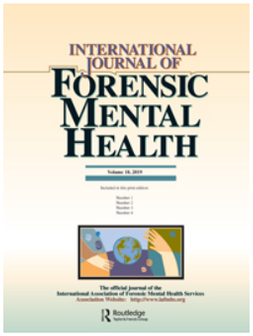

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Some Ethical Considerations About the Use of Biomarkers for the Classification of Adult Antisocial Individuals

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ABSTRACT

It has been argued that a biomarker-informed classification system for antisocial individuals has the potential to overcome many obstacles in current conceptualizations of forensic and psychiatric constructs and promises better targeted treatments. However, some have expressed ethical worries about the social impact of the use of biological information for classification. Many have discussed the ethical and legal issues related to possibilities of using biomarkers for predicting antisocial behavior. We argue that prediction should not raise the most pressing ethical worries. Instead, issues connected with "biologization", such as stigmatization and negative effects on self-image, need more consideration. However, we conclude that also in this respect there are no principled ethical objections against the use of biomarkers to guide classification and treatment of adult antisocial individuals.

KEYWORDS

Classification of antisocial behavior; biomarkers; bioprediction; ethical issues; stigma

Introduction

Many individuals with an antisocial personality present a social problem that requires an appropriate response. Such individuals are typified by antisocial tendencies, such as lack of inhibition, extreme violence, and aggressive behavior. Studies indicate that around 50% of the world's prison population is comprised of individuals with antisocial personality disorder (ASPD) (Fazel & Danesh, 2002), a broad and heterogeneous psychiatric diagnosis capturing elevated proneness toward exhibiting severely antisocial behaviors. In the United States, it is estimated that among the individuals with ASPD, 15–20% also satisfy criteria for psychopathy (Hare, 2003), an even more severe personality disorder characterized by lack of empathy, remorse, and guilt, in addition to the more common antisocial behaviors. Moreover, individuals with psychopathic traits are disproportionately more likely than any other group of people to commit a crime and violently recidivate (Kiehl & Hoffman, 2011). In this respect, they put enormous pressure on our moral, legal, and economic systems (Kiehl & Buckholtz, 2010).

Recently, Brazil and colleagues (2018; see also Blair, 2015) have proposed a biomarker-informed classification to replace the current classifications of antisocial individuals. Biomarkers are objective and measurable characteristics of biological processes that are used for identifying normal and pathological processes and responses to different types of medical intervention. These characteristics can include everything from gene expression, blood and pulse pressure, brain activation patterns, or any other measurable process or substance in the body that affects patients' health. Current classifications of antisocial individuals, with their over-reliance on behavioral tendencies, fail to capture the large amount of heterogeneity in antisocial populations. This has precluded the rapid development of effective responses and therapies for these individuals (Brazil, van Dongen, Maes, Mars, & Baskin-Sommers, 2018). The potential of using biomarkers has received a large amount of attention and has even led to the

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development of frameworks such as the Research Domain Criteria (RDoC), that aim to redefine the way psychiatric conditions are viewed (e.g., Buckholtz & Meyer-Lindenberg, 2012; Insel et al., 2010). The common aspiration in these proposals is overcoming the limitations of relying solely on observed behavior to generate syndrome-based diagnoses, which is the approach used in currently dominant classificatory systems, such as the Diagnostic Statistical Manual (DSM: American Psychiatric Association, 2013) and the International Statistical Classification of Diseases and Related Health Problems (ICD; World Health Organization, 1993).

The introduction of biomarkers for antisocial personality disorders, despite its potential benefits, has raised several ethical concerns (Singh & Rose, 2009). Some have considered the possible disruptive consequences of such classification for current moral and legal practices of prediction of antisocial behavior (Aharoni et al., 2013; Nadelhoffer et al., 2012; Nadelhoffer & Sinnott-Armstrong, 2012; Poldrack et al., 2018; Singh, Sinnott-Armstrong, & Savulescu, 2014). Other ethical problems about biomarkers might be raised by the consequences of what can be called the "biologization" of antisocial behavior (Horstkötter, Dondorp, & de Wert, 2015). These issues involve the dangers of medicalization of deviant behavior, the stigmatization, and the negative self-image that might derive from the use of such classifications (Pickersgill, 2011; Sadler, 2008).

In this article, we argue that the introduction of biomarker-based classification of antisocial behavior in adults should not attract these ethical worries. With regard to the ethical and legal issues of using biomarkers for predicting antisocial behavior, we recognize their importance and discuss some open issues. However, we maintain that the problem of how "biologization" relates to stigmatization and negative self-image deserves more attention. One dimension of this problem is descriptive and concerns whether and how these classifications induce stigmatization and negative self-image and how they will or might be used in moral, forensic and legal practices. In this article, we do not address this dimension of the problem. We consider, instead, the conceptual or normative issue whether there is any rational ground for concluding that a biomarker-based classification should imply stigma or affect adversely self-image. We respond in the negative by arguing that associations between biologization, stigmatization, and related negative self-image are empirically and normatively, unjustified.

In the next sections, we will review some problems related to the current systems of classification and highlight how the field might benefit from devising classifications informed by biomarkers. Then, we consider some worries about the prospects of using biomarkers for prediction of dangerous behavior. Finally, we reflect on some ethical implications of introducing biomarker-informed classification as they relate to "biologization" of antisocial behavior.

It is important to first point out that the scope of this article is limited to the use of biomarkers for classifying adult antisocial individuals. Although an increasing amount of attention is paid to the ethical aspects that are related to the treatment and classification of antisociality among the youth (Baum & Savulescu, 2014; Horstkötter et al., 2015), there are multiple factors that force us to be cautious about generalizing our claims across different age cohorts. One reason is that, due to the complexities of maturation, it is difficult to predict which children with conduct problems become antisocial adults. In fact, a portion of children with early-onset conduct problems desist when they reach adulthood (e.g., van Domburgh, Vermeiren, Blokland, & Doreleijers, 2009), indicating that factors such as brain maturation, environmental changes, epigenetic changes, and so on, can affect a child's developmental trajectory significantly (Brazil, 2015; Fontaine, Rijsdijk, McCrory, & Viding, 2010). Another factor is that the operationalizations of antisocial personality constructs differ between children and adults. For instance, the construct of psychopathy, denoting a severe type of antisocial personality, includes interpersonal facets (such as manipulative behavior, pathological lying, and glibness), while the children's analogue of the psychopathy construct does not (Hare, 2003; Viding & McCrory, 2012). This fact introduces conceptual mismatches between the age cohorts whose relevance and implications have not been sufficiently investigated. These examples highlight that it is important to remain cautious when generalizing across age cohorts. To avoid further confusions, and in accordance with prior suggestions based on discordant patterns of empirical results between antisocial adults and youth (see Hoppenbrouwers, Bulten, & Brazil, 2016), this article will be limited to adult antisocial individuals.

Problems in the current systems of classification of adult antisocial individuals: psychopathy as an example

Currently, most personality disorders, including the antisocial personality disorder, are classified by scoring observed behavior and using these scores to make inferences about unobservable characteristics such as personality traits. Some of the general reasons for

dissatisfaction with this type of syndrome-based classifications, as captured by the DSM 5 and ICD, are heterogeneity, low construct validity, and the categorical measurement of disorders (Lilienfeld, 2014; Lilienfeld, Smith, & Watts, 2013; for a philosophical discussion, see Murphy 2009). Many constructs of mental disorders capture heterogeneous behavioral and personality features that cluster together conditions with diverse sets of symptoms and etiologies. Such constructs tend to have low validity because they are not very good at predicting external criteria, such as etiology, performance in experimental tasks, and responsiveness to treatment. Finally, DSM conceptualizes disorders as being clearly outlined, that is, as having a categorical structure (Haslam, 2014), while research indicates that most disorders in currently available syndrome-based diagnostic systems have a dimensional structure (Haslam, Holland, & Kuppens, 2012). To further research in this area, many suggest introducing a more data-driven classification system of psychopathology (e.g., Buckholtz & Meyer-Lindenberg, 2012; Insel et al., 2010; Lilienfeld, 2014; Stephan, Iglesias, Heinzle, & Diaconescu, 2015).

Problems related to syndrome-based classification spill over to the study of antisocial behavior (Skeem, Polaschek, Patrick, & Lilienfeld, 2011). The most pressing issue in this regard is that there is currently no effective therapy for reducing or preventing antisocial behavior correlated with psychopathy and other antisocial personality types (Brazil et al., 2018; Salekin, Worley, & Grimes, 2010; cf. Baskin-Sommers, Curtin, & Newman, 2015). The reason for the lack of therapeutic success seems to lie (at least in part) in the heterogeneity and the lack of external validity of the construct of antisocial personality and its subtypes. Psychopathy offers a clear example of the struggle for finding the best way of classifying individuals with antisocial personality structures. The history of psychopathy is permeated with different conceptualizations, which led to different tools and approaches for measuring psychopathy (Pickersgill, 2012; Skeem et al., 2011). For instance, Karpman (1941) distinguished between primary and secondary psychopaths based on their assumed differences in etiology. He considered primary psychopaths to be those whose psychopathic traits and antisocial behavior is genetically determined. Secondary psychopaths are supposed to be those whose antisocial behavior is mainly a product of social environment. More recently, the primary/secondary distinction was alternatively defined in terms of variations in anxiety levels. From this perspective, individuals with psychopathic traits who exhibit low levels of anxiety are labeled primary and those who exhibit higher levels are labeled secondary psychopaths (Lykken, 1995). These examples indicate that there are different subtypes of psychopathy that are likely to differ in their etiology. Importantly, these distinctions should be reflected in our classification systems, which would enable devising more effective and selective diagnostic and treatment tools, and public policies (Brzović, Jurjako, & Šustar, 2017; Gonzalez-Tapia, Obsuth, & Heeds, 2017).

Furthermore, there is disagreement on what the core traits of psychopathy are and how to measure them (Lilienfeld, 2013). For instance, some insist that antisocial behavior belongs to the construct of psychopathy (Hare, 2003), while others think that antisocial behavior might be correlated with psychopathy, but it is not a core feature (Cooke & Michie, 2001; Međedović, Petrović, Kujačić, Đorić, & Savić, 2015). These conflicts in conceptualizations of psychopathy led to devising different measures and conceptualizations of psychopathy (for an overview see Brazil & Cima, 2016; Brazil et al., 2018). For instance, some researchers emphasize the distinction between successful and unsuccessful psychopaths (Glenn & Raine, 2014). Successful psychopaths are supposed to be characterized by elevated interpersonal (e.g., deceitful, manipulative, liars) and affective (unempathic, callous, glib, etc.) traits, but they do not exhibit extreme antisocial and violent behavior. Unsuccessful psychopaths are supposed to be those who also possess, to a relatively higher degree, antisocial and impulsive traits.

Different conceptualizations and measurements of psychopathy have led to divergent results with respect to its external correlates. A highly indicative example of this is Baskin-Sommers et al.'s (2015) study where they show that the same group of incarcerated psychopathic offenders, depending on which measure of psychopathy is used, exhibit different correlations with executive functions. Among other things, their study showed that a self-report scale capturing Fearless Dominance, a broad construct believed to measure the core interpersonal-affective features of psychopathy, correlated positively with task-based measures of executive function in a group of offenders. In contrast, no correlations were found between executive function and core interpersonal-affective psychopathic traits measured with another instrument known as the Psychopathy Checklist-Revised (PCL-R; Hare, 2003) in the same group. This example illustrates how the instruments used in a study can affect empirical results.

Thus, the different attempts at characterising psychopathy are clear manifestations of the ongoing struggle to find better ways to operationalize antisocial personality constructs. It is likely that this challenge, as well as a lack of external validity and robust correlations with different neurocognitive deficits, has hindered devising efficacious treatment. A promising way out of these methodological and research difficulties is to take a more data-driven or bottom-up approach (e.g., Insel & Cuthbert, 2015; Lilienfeld, 2014; Stephan et al., 2015). Numerous genetic, developmental, and neuroscientific studies correlate various aspects of antisocial behavior with neurocognitive abnormalities and deficits (for a survey, see Brazil et al., 2018). Instead of trying to ground different psychologically or behaviorally defined symptoms of antisocial and psychopathic behavior in biological and cognitive (i.e., biocognitive) data, the alternative is to start with the biological and cognitive data that are correlated with antisocial behavior and rebuild the classification bottom-up.

The biocognitive approach to classification of antisocial behavior

Given the very limited successes in treatment, and psychometric results pointing to the heterogeneity among antisocial individuals, many researchers are proposing biology and cognition based classifications (Blair, 2015; Brazil et al., 2018; Buckholtz & Meyer-Lindenberg, 2012, Stephan et al., 2015). Brazil and colleagues (2018), inspired by the NIH's Research domain criteria (RDoC) project (Insel et al., 2010), propose to rebuild the classification of antisocial individuals by relying on genetic, neurobiological, and cognitive data obtained from individuals that engage in antisocial behavior.

The envisioned reclassification cannot avoid beginning with antisocial behavior that is delineated by relying on common practices. This includes delineating a group of individuals that have consistently shown disruptive behaviors that deviate from the societal norms (Sadler, 2008). At this stage, antisociality is clearly demarcated by moral and social criteria, since these individuals are normally individuated among the people who are already committed to forensic institutions due to exhibiting repeated and severe forms of antisocial behavior (Pickersgill, 2012). In addition to the traditional symptom-driven and psychology-based diagnostic manuals, such as the DSM's construct of antisocial personality disorder and Hare's Psychopathy checklist (Hare, 2003), or the more recent Triarchic model of psychopathy (Patrick, Fowles, & Krueger, 2009), Brazil and colleagues (2018) propose to use biomarkers correlated with different forms of antisocial behavior to produce what they call specific *biocognitive fingerprints* of antisocial offenders.

Biocognitive fingerprinting integrates different types of data spanning from genetics, neuroimaging and cognitive/behavioral studies, to obtain a better description of the commonalities and differences between various types of antisocial individuals. This approach involves using data mining algorithms that, by combining different types of data, identify combinations of (neuro)biological and genetic markers to build biocognitive profiles that best describe individuals with similar biocognitive characteristics, while at the same time maximizing the difference with individuals with other biocognitive profiles. Within a profile, an individual is scored along the axes of the relevant dimensions included in the biocognitive profile, thus creating a unique signature or biocognitive fingerprint, for each individual (see Figure 2 in Brazil et al., 2018).

There are increasing data that suggest that neurobiological and cognitive dysfunctions distinguish psychopathic behavior from other forms of antisocial behavior (Brazil, 2015). For example, studies indicate that psychopathy, as measured by the PCL-R, is linked to abnormal functioning of brain regions that subserve emotional processing underlying empathic reactions, decision-making, and moral judgment (e.g., Anderson & Kiehl, 2012; Blair, 2013). Most notably, the amygdala, the ventromedial (VMPF) and orbitofrontal cortex (OFC) (Blair, 2008), and the extended neural circuitry that is related to the broader paralimbic area of the brain (Kiehl, 2006) are among these regions. Functional MRI research also found, for example, reduced activity in the anterior cingulate cortex, the anterior insula and ventral striatum in offenders with comorbid ASPD and psychopathy relative to those with only ASPD (Gregory et al., 2015; Hosking et al., 2017). The correlation of psychopathic traits with dysregulation of attentional processes is another prominent example of cognitive deficiencies believed to differentiate this group from other antisocial populations. When psychopaths' primary attentional focus is directed to a response set (perceptually accessible choice options), then the secondary or peripheral stimuli that are outside of that response set do not impact their decision-making processes. This could account for the disinhibition and maladaptive decision-making often seen in psychopathy (Koenigs & Newman, 2013). In sum, these studies indicate that

psychopathic antisocial behavior can be conceptualized and classified along the lines of dysfunctions in different (neuro)biological and cognitive systems (see, also, Hamilton, Hiatt Racer, & Newman, 2015), and that the nature of these impairments seem to distinguish among groups to some extent.

Interestingly, there are some preliminary, but very promising results of therapies targeting cognitive functions to mitigate dispositions underpinning antisocial behavior. Cognitive remediation therapy (CRT) is a tailored approach to treatment that aims to improve cognitive skills (e.g., attention, memory) by letting patients repeatedly perform tasks that engage the target cognitive functions that require enhancement or better regulation. Baskin-Sommers, Curtain and Newman (2015) designed a CRT-based intervention to improve cognitive deficits that are specific to psychopathic and non-psychopathic offenders, respectively. Their approach was based on the evidence showing that psychopaths exhibit deficits in modulating attention when there are multiple sources of information needed to solve a task, while other offenders exhibit aberrant responses to affective and motivationally relevant stimuli, but not in modulating attention. The therapy consisted of a condition in which trainings matched deficits associated with each of the two groups of offenders and a condition in which trainings meant for attention processing were applied to offenders with aberrant affective processing and *vice versa*. They found significant improvement of the targeted cognitive functions, but only when the training matched the cognitive deficit typical of the specific group (i.e., attention vs. affective regulation).

These results are promising, and indicate that classifying and studying antisocial offenders according to their biocognitive characteristics may facilitate the development of more tailored treatments for other deficiencies too. Still, it is important to consider potential ethical consequences of such endeavours. In the next section, we begin discussing some ethical worries that these types of approaches may bring about.

Ethical concerns about the bioprediction of antisocial behavior

Several authors have raised and discussed ethical worries concerning predicting criminal or other kind of harmful behavior on the basis of biomarkers (Nadelhoffer et al., 2012; Nadelhoffer & Sinnott-Armstrong, 2012; Poldrack et al., 2018; Singh et al., 2014). In this regard, the MAOA gene, which was initially found to be highly correlated with antisocial behavior, has long been considered a potential biomarker for antisociality, and has captured the attention of many ethicists (Baum, 2013; Baum & Savulescu, 2014). The MAOA gene has long and short variants and encodes a monoamine oxidase A enzyme that regulates monoamine neurotransmitters, such as dopamine, serotonin and norepinephrine. The main function of the MAOA enzyme is to decompose monoamine neurotransmitters. There is evidence that dysregulated production of serotonin is correlated with impulsive and violent behavior (Coccaro, 1989). Thus, failures of MAOA gene to produce enzymes that regulate the production of serotonin seem to be (partly) responsible for a higher risk for violent behavior in individuals with mutations in the MAOA gene (Brunner, Nelen, Breakefield, Ropers, & van Oost, 1993).

The discovery of the links between the MAOA gene and antisocial behavior sparked considerable discussion on the ethical implications of using this gene as a biomarker for predicting risk of developing disorders and for predicting future behavior. One key finding is that individual biomarkers seem to have little predictive power (Singh & Rose, 2009; Brazil et al., 2018). For instance, Caspi and colleagues (Caspi et al. 2002) provided evidence that only the long variant of the MAOA gene is a predictor of greater risk for antisocial behavior, but only among individuals who suffered from serious forms of abuse during childhood. In addition, genes that correlate with psychopathology often have pleiotropic effects that cut across current psychiatric taxonomy (Buckholtz & Meyer-Lindenberg, 2012). This means that the same gene expression patterns can have similar or different (neural) manifestations, depending on the environmental conditions and the way these interact with genes. This could be one explanation for another, more specific, problem pertaining to the current lack of robustness of the genetic and neuroscientific data.

Empirical findings justify ethical concerns about the suitability of using current biological information, such as expression of the MAOA gene, to discover biomarkers that help classify, treat, predict and respond to antisocial behavior. However, worrying about the possible consequences of reliable bioprediction is premature. In fact, different studies have shown opposite correlations between different variants of the MAOA gene and antisocial behavior. Some studies have failed to replicate positive correlation between the gene and antisociality (Haberstick et al., 2005; Huizinga et al., 2006). Furthermore, mutations

in the MAOA gene have been associated with psychiatric conditions that are not typically linked to antisocial personality, such as autism, schizophrenia, depression and bipolar disorder (Buckholtz & Meyer-Lindenberg, 2014). The inconsistent results regarding the MAOA gene is only one example of how the search for individual genes that can be used as biomarkers for psychopathology has failed to deliver the expected results. It seems likely that the heterogeneity among individuals showing antisocial behavior will preclude the identification of isolated genes that can serve as biomarkers in the near future.

In general, assessing whether the application of bioprediction in many legal and social practices is premature involves addressing several issues. Firstly, there are relevant legal debates aimed at establishing when scientific predictive information, not necessarily of a biological kind, can be usefully used for initial sentencing, parole or rehabilitation monitoring (Douglas, Pugh, Singh, Savulescu, & Fazel, 2017; Hübner & White, 2016; Pugh & Douglas, 2016). Secondly, the ethical justification of application of bioprediction in particular might tolerate different reliability thresholds depending on the specific context and the balance of values at hand. Generally, the conflicting values tend to oppose the interests of an individual patient or offender and the interests of the wider public (Douglas et al., 2017). Depending on the context we might give more weight to one value over the other and accordingly tolerate prediction tools with specific features. For instance, when deciding on a preventive commitment to a psychiatric or prison institution of a person who has already served her full sentence we should rely on tools and data that minimize the rate of false positives. Namely, we should avoid assessment tools that could prolong incarceration of those who bear predictive markers but are not prone to violent behavior anymore. On the other hand, when deciding on a parole release, even if we mistakenly predict that an individual will continue to be violent still the incarceration time would be within the limits of the original sentence. Thus, in the parole case, we might prefer tools and data that minimize the rate of false negatives because we might give more precedence to securing the public safety (Douglas et al., 2017).

Nonetheless, regarding adults, bioprediction practices that would involve serious involuntary interference on personal freedom such as preventive incarceration, sentencing based on risk assessment, and mandatory treatments appear to be premature. In fact, arguably, these practices have and ought to have a very low tolerance for predictive error (Eastman & Campbell, 2006; Hübner & White, 2016). Without giving an exhaustive discussion, there are at least four sets of reasons indicating that presently most methods for predicting risky antisocial behavior, including bioprediction, do not satisfy such a requirement (see also Poldrack et al., 2018). Let us consider them.

The first set of reasons emerges within the issue of extrapolating group-level knowledge to generate inferences about the individual (Dawid, 2017). An important aspect of this problem is that the law targets the propensity of an individual to commit some unlawful action in the future, or her legal responsibility for a specific action. In contrast, scientific investigations commonly use data that are aggregated across individuals to reach general conclusions about the features exhibited by whole populations (Eastman & Campbell, 2006). Buckholtz and Faigman (2014) have given a hypothetical example of the problem caused by 'group-to-individual' extrapolation, in which they examined results from neuroimaging studies of lying. At the group level, lying seems to be associated with increased activity in the dorsolateral prefrontal cortex (DLPFC). However, not every individual who lies exhibits this neural pattern. Some do not exhibit this pattern at all, while some even exhibit the opposite pattern of activity in DLPFC. Focusing on the average DLPFC activation across individuals will obscure the detection of the individual differences. Thus, group average data do not guarantee conclusions about all individuals who form the group.

The second problem with the bioprediction of criminal behavior stems from more general methodological challenges in the empirical research. Current actuarial risk-assessment tools have a large margin of error when they are applied to obtain risk estimates of individuals' propensity for future violence (Douglas et al., 2017; Hart, Michie, & Cooke, 2007). Large margins of error make it difficult to estimate with certainty the probability that an individual will act violently. Thus, Hart et al. (2007) warn that risk-assessment tools should be used with great caution or not used at all. Similar issues may be raised regarding the inclusion of biomarkers for estimating an individual's risk for engaging in violent behavior (for a discussion, see Monahan, 2014).

A third issue is that science and the law use different levels of description and explanation of human behavior (Buckholtz & Faigman, 2014; Francken & Slors, 2018). The law uses higher-order constructs such as 'justice', 'social dangerousness' or 'responsibility' that apply to the level of a person, while neuroscientists talk about neurons and neural

networks that are described in biochemical and mechanistic terms (Campbell & Eastman, 2014). Often, it is not clear how constructs from one level or domain should be translated and implemented in the other (Buckholtz & Faigman, 2014; Jurjako & Malatesti, 2017). Thus, often the correlation of biomarkers with some behaviors has not clear implications for higher-order legal constructs. Similar considerations apply to predicting dangerousness in legal contexts based on biomarker information. If there is uncertainty about the proper translation of biomarker information into higher-order or legal terms, then there is a potential danger of misconstruing the relevance of this information in legal and social practices. These issues are all relevant in the context of the admissibility of evidence in legal proceedings, where standards of permissible evidence tend to be more stringent given the greater preference of the courts for avoiding punishing the innocent instead of the guilty (Campbell & Eastman, 2014). In this context, the dangers of using biomarkers include creating a wrong impression of their reliability and relevance for prediction that people intuitively, although without proper grounds, impute to scientific results that utilize this vocabulary.

The inappropriate use of biomarkers of antisocial behavior in the present context might lead to the further problem of committing the so called "psycho-legal fallacy". This is the mistake of assuming that "identifying a biomechanical cause by itself excuses behavior" (Aspinwall, Brown, & Tabery, 2012, p. 847). Given that, ultimately, all behavior is underpinned by some causal factor, this claim would imply that nobody is accountable for his/her behavior (see Morse, 2000). One variant of the psycho-legal fallacy is thinking erroneously that any kind of salient structural brain difference indicates a legally relevant impairment or incapacity. Determining dangerousness of an individual and reliably predicting his/her behavior requires establishing whether the offender had the relevant capacity to control his/her actions (Poldrack et al., 2018). This cannot always be established just by using biological and cognitive data. For instance, patients whose Corpus Callosum (a bundle of fibers connecting the brain hemispheres) had to be surgically removed and those who are born without it have similar brain structures. Nevertheless, because of the brain's plasticity, cognitive functions relying on the Corpus Callosum can be carried out by other brain structures. Thus, despite having similar brain morphology, individuals born without Corpus Callosum are less cognitively and behaviorally impaired than patients who had it removed due to illness (Jeeves, 1996). This indicates that not every brain difference is pertinent to establish whether a legally relevant capacity is present (see Jurjako & Malatesti, 2018).

The fourth set of reasons for scepticism about bioprediction of antisocial behavior arises from the fact that current empirical research indicates that most psychiatric disorders, as currently conceptualized, denote heterogeneous causal and symptomatic structures (Haslam et al., 2012). If it were the case that psychiatric disorders denote "distinct, independent [entities] with a unique set of causal factors and pathophysiological processes" (Buckholtz & Meyer-Lindenberg, 2012, p. 993), then there would be a greater chance of finding biomarkers that could uniquely predict features related to that disorder. However, it is generally recognized that most psychiatric disorders exhibit a dimensional structure (Baum, 2016; Buckholtz & Meyer-Lindenberg, 2012). This explains why in current taxonomies of psychopathology in general, and taxonomy of antisocial personality disorders in particular, there will be biomarkers that are common to many different conditions and disorders that do not necessarily share other personality or behavioral features (Buckholtz & Meyer-Lindenberg, 2012; Lilienfeld, 2014). Thus, we should not expect that certain biomarkers will have high predictive value given our current taxonomy of disorders. The main reason seems to be that current approaches to distinguish among antisocial individuals are based on behaviorally defined categorizations, insofar they involve the description of specific behaviors and a reliance on behavior to infer mental states and personality traits, which do not often map onto unique or nicely delineated biological processes, mechanisms, or traits (Poldrack et al., 2018).

All these issues indicate that using biomarker-informed classification for prediction of future behavior might be premature. Importantly, however, we do not claim that biomarkers should not be used at all for prediction or that they are useless in this respect (cf. Baum & Savulescu, 2014). For instance, the predictive power of biomarkers is increased when they are combined with other risk factors and environmental data, such as family history (Singh & Rose, 2009). In this regard, a great deal of ethical reflection has already been devoted to thinking and devising social policies for early prevention in children at risk of engaging in severe antisocial behavior (Baum & Savulescu, 2014; Horstkötter et al., 2015).

To sumarize, the research on bioprediction of antisocial behavior, despite its intrinsic and instrumental value, presently does not appear to offer results that

imply a significant impact on our legal and other normative practices (for suggestions how to improve the practices of bioprediction, see Poldrack et al., 2018). Thus, although we do not dismiss the relevance of ethical reflection on the appropriateness of using biomarkers for prediction, there might be other uses of biomarkers that deserve to be objects of ethical investigation. In the next section, we will examine some ethical issues related to using biomarker-informed classifications.

Some ethical issues regarding the biocognitive reclassification of antisocial behavior

Some scholars have expressed worries about the "biologization" of mental disorders (e.g., Haslam, 2014; Pescosolido et al., 2010; Phelan, 2005). There are some principal concerns about "biologization". First, one worry about biologization is that it creates a false impression that forensic and psychiatric conditions can be reduced to clearly delineated biological categories. In fact, the prospects of successfully grounding psychiatric classifications on biological factors are not good because most mental disorders, as they are *currently* classified and conceptualized, are heterogeneous and exhibit a dimensional structure (Haslam et al., 2012). However, the goal of biology-informed proposals for the classification of antisocial behavior is not to "biologize" *current* classification systems of mental disorders, but rather to encourage a *reclassification* of antisocial behavior based on biocognitive data. This could include devising new categories of subtypes of antisocial behavior with a prospect of individualization and creation of biocognitive fingerprints of groups of antisocial offenders that would enable tailor-made therapies (Brazil et al., 2018).

Worries about the medicalization of antisocial behavior

A related worry is that reliance on biomarkers will encourage illegitimate forms of medicalization. Ethical and empirical issues related to medicalization are multifaceted (Rose, 2007). In our case, the worry might be that biomarker-based classification forces "understanding of behavior as mainly caused by various biological features" (Horstkötter et al., 2015, p. 288) that require medico-pharmacological solutions and therapies (Pickersgill, 2011; Rose, 2007).

There are two important considerations that alleviate the seriousness of this worry. First, it seems that medicalization is considered morally dubious mostly when there are available other, non-medical forms, of treatment that reduce problems by reducing social and environmental factors underpinning some problematic condition (Horstkötter et al., 2015). In the case of the most severe forms of antisocial behavior, there seem to be no known feasible therapies that solely rely on reducing the environmental risk factors. This is one of the reasons for thinking about reconceptualization of the category according to certain salient biomarkers (Brazil et al., 2018; see also Pickersgill, 2011). Moreover, supporters of therapies based on biocognitive fingerprinting neither necessarily utilize medico-pharmacological means nor downplay the importance of the environmental factors (Pickersgill, 2009). In fact, the above-mentioned cognitive-remediation therapy study (Baskin-Sommers et al., 2015), for example, is based on the knowledge of cognitive mechanisms that differentiate between two groups of individuals with antisocial personality structures. Thus, no medical or pharmacological compounds were required for successful treatment to occur.

Stigmatization and biomarker-based classification of antisocial behavior

Another kind of worry concerns the practical consequences of adopting a more biologically informed taxonomy. In the case of the framework proposed by Brazil et al. (2018), these worries are most notably related to the stigmatization of individuals classified by using biocognitive fingerprints. Stigmatization in this context refers to the social consequences of using labels that might have socially undesirable implications for the groups of people receiving such labels. A related problem is that being so labeled might negatively affect the self-image of the individual. Before addressing these issues, some clarifications are needed.

Clearly, we should distinguish between justified forms of censorious and punitive social responses that would in certain ways set individuals apart from the rest of the society, and unjustified forms of stigma. Individuals prone to severe antisocial behavior will be rightly a target of certain restrictive measures for their misconduct because they violate other people's rights and undermine the norms of fair cooperation (Baccarini & Malatesti, 2017; see, also, Glenn, Focquaert, & Raine, 2015). We expect that biomarker-based classification will improve the chances of devising, in principle, just responses to such individuals in terms of effective treatment and rehabilitation opportunities. However, they should not be stigmatized

because of misconceptions about the nature of biomarker information pertaining to each individual.

There is some empirical evidence that might authorize the conclusion that biomarker-based classification might exacerbate the stigmatization of antisocial individuals. For instance, former offenders, who are labeled as such, have difficulty finding employment, housing, and successfully reintegrating into the normal fabric of social life. These factors are all correlated with recidivism (Chiricos, Barrick, Bales, & Bontrager, 2007). Some studies show that using biological explanations of mental disorders make people less inclined to ascribe responsibility and blame to the patients, but they also express fear related to their unpredictability and dangerousness, and thus a preference for more social distance from the patients (Kvaale, Gottdiener, & Haslam, 2013). It is important to stress that these researches concern mostly depression and schizophrenia. Regarding adults with antisocial personality, studies indicate that people perceive a specific individual that has been described as having psychopathic traits as being more prone to engage in antisocial behavior in the future (e.g., Aspinwall et al., 2012; Edens, Desforges, Fernandez, & Palac, 2004, Edens, Colwell, Desforges, & Fernandez, 2005).

Some limited empirical evidence discourages assuming that biomarker-based classification might have negative effects on self-image. In a landmark pilot study, Horstkötter and colleagues (2012) found that juvenile delinquents do not exhibit negative self-image effects that would lead to self-fulfilling prophecies, even when their diagnoses were correlated with biomarkers such as low cardiac activity. Although the juveniles in the study expressed concerns about possible stigmatization, they did not see their psychiatric diagnoses as part of their personalities. Nor did they rationalize or explain their criminal behavior by using psychiatric diagnoses. Instead, the diagnoses were "meaningless to them" (Horstkötter, Berghmans, de Ruiter, Krumeich, & de Wert, 2012, p. 291). New empirical studies on self-image and stigmatization might further show how biocognitive classification and explanations of antisocial behavior may influence self-image.

Biocognitive classifications and essentialism

Besides researching empirically whether people might associate biocognitive classifications with stigma and negative self-image, there is another relevant line of investigation. We should also investigate which reasons might lead people to associate biomarker-based classification with unjustified stigma and negative self-image. Let us consider which type of considerations might support such an association.

Some claim that devising biocognitive classifications of antisocial behavior might encourage *essentialist* thinking about these conditions (Dar-Nimrod & Heine, 2011; Haslam, 2011, 2014; Phelan, 2005). Essentialism implies that all behaviors related to mental disorders depend on a fixed and immutable nature. This view derives from the fact that people tend to essentialize many everyday categories that govern our thought and actions (Gelman, 2003). For instance, according to Haslam "people tend to believe that some social categories—especially those based on gender, race, and ethnicity—have defining properties and are biologically based, discrete, historically invariant, and immutable" (Haslam, 2014, p. 23). These attitudes toward social categories have ethically negative effects since they increase racial and gender-based prejudice, reinforce social divisions and antagonistic attitudes towards outgroup members (Dar-Nimrod & Heine, 2011). Similar attitudes get reinforced regarding psychiatric conditions, in which case the explanation would be that lay people tend to essentialize mental disorders as categorical and discrete and underpinned by biological causes (Dar-Nimrod & Heine, 2011; Hinshaw, 2007).

Thus, the worry might be that attempting to reclassify different disorders along the lines of current knowledge of biocognitive signatures correlated with different symptoms "is likely to encourage stigma because it represents sufferers as categorically abnormal, immutably afflicted, and essentially different" (Haslam, 2014, pp. 24–25). In addition, it might encourage in the society at large regarding such behaviors as predetermined and antisocial individuals as natural born criminals (Glenn et al., 2015; Jalava, Griffiths, & Maraun, 2015). Furthermore, the pessimism about treatability of biologically or cognitively construed disorders might, in turn, affect self-identifying beliefs and self-image of individuals with psychiatric diagnosis in a way that triggers self-fulfilling prophecies (Kvaale, Haslam, & Gottdiener, 2013).

However, finding biocognitive signatures does not sit well with psychological essentialist prejudices. The studies on biomarkers are not primarily about the genetic make-ups that determine antisocial behavior. In that regard, there is no inclination towards genetic determinism (Buckholtz & Meyer-Lindenberg, 2014). This research program also incorporates insights from studies indicating that antisocial behavior is a result of a complex interaction between environment, genes,

and neurodevelopmental factors (Brazil, 2015). Even in the case of psychopathy, whose core traits seem to have a genetic basis, antisocial behavior seems to be a product of those genes in combination with external factors such as having an adverse early childhood (Gao, Raine, Chan, Venables, & Mednick, 2010). Furthermore, biocognitive fingerprints mostly denote correlations, and not causal factors, that necessarily lead to antisocial behavior. In this respect, there is also no inclination for thinking that whatever biomarkers are found will deterministically influence the behavior of individuals.

It might be objected that the promise of the biomarker-based classification for devising effective therapies can only be delivered on the supposition that biomarkers deterministically cause antisocial behavior. If the etiology of antisocial behavior involves complex interactions between the environmental, developmental, and biocognitive factors, then reclassifying antisocial individuals according to specific biomarkers cannot be expected to produce better therapies. This objection, however, presupposes that the only way of treating a condition is by acting on its total causal etiology.

However, this is not the case. For instance, a person might experience different kinds of physical and psychological distress due to paraplegia. Given that we have no effective medical therapy for removing the main cause of the person's distress, we still have options for alleviating his/her distress. Most notably, this involves adjusting the social and physical environment so to adapt it to his/her needs. Similarly, the proposal to reclassify antisocial individuals based on their biocognitive features ultimately aims to uncover biocognitive profiles of different types of traits correlated with antisocial behavior, which can be used to develop suitable individualized therapies that are currently lacking (Brazil et al., 2018). This approach enables us to target specific features underlying antisocial behavior in a piecemeal fashion, disentangling proximal and distal factors that comprise the complex biosocial underpinnings of different forms of antisocial behavior. For instance, knowing that some subgroup of psychopaths exhibits deficits in decision-making that are correlated with specific attentional and neural aberrations (Moul, Killcross, & Dadds, 2012) enables us to try to devise techniques for reducing these specific aberrations that influence maladaptive behavior (Baskin-Sommers et al., 2015). This way of proceeding does not presuppose that we act on the total complex causal process underlying the etiology of severe forms of antisociality.

Biomarkers and opportunities for change

Biocognitive fingerprinting should not have negative stigma effects because, in general, having the opportunity to represent biocognitive traits underlying one's condition as external to the self may enable an individual to take measures against it (Ross, 2007; cf. Malatesti & Jurjako, 2016, p. 94–96). For instance, discovering that mood changes are mainly due to a chemical imbalance in the brain enables the person to take control over it and act on the causes of his/her undesirable condition. Something he/she could not have done before this information was acquired. Similarly, if attentional deficits and its underlying neural correlates affect psychopaths' maladaptive behavior, then learning about and objectifying it can be used by an individual to try to remedy it through therapy (see Baskin-Sommers et al., 2015). Thus, learning about biocognitive correlates or causes of one's behavior can help to objectify the problem, and motivate the individual to try and find a solution for it.

It should be acknowledged, however, that the latter might not apply to all forms of antisocial behavior. For instance, it is an open issue whether psychopathic individuals who, due to their lack of empathy, guiltlessness, grand sense of self and defiant attitudes, would be prone to actively engage in remedying their behavior through therapy (Hübner & White, 2016; for other challenges of this type, see Poldrack et al., 2018). In this regard, some authors and studies provide more optimistic results (Horstkötter et al., 2012). In fact, some experts indicate that, despite negative impressions, such individuals would be willing or more motivated to actively engage in different forms of therapies that aim at modifying the antisocial aspects of their behavior if it is made clear to them that the therapy and the modifications it will lead to are in their best interest (Hare, 2003).

Others, more pessimistically, maintain that for psychopaths to be motivated to take control of the biomarkers that influence their antisocial behavior amounts to thoroughly changing personalities or "world views" of psychopathic individuals (Maibom, 2014). However, in that case, we would be entitled to react to them with justified forms of disapproving attitudes. Not because biomarkers associated with psychopathic and antisocial traits are essential or immutable. But because our moral and legal practices would treat such persons as *choosing* behaviors and ways of life (Jurjako & Malatesti, 2017) that cause in others understandable and justifiable attitudes of fear and a preference for social distance, which are often used in

the operationalization of stigma (Haslam, 2014). Thus, due to their criminal and non-cooperative behavior, certain discriminatory reactions, such as restrictions of freedom and opportunities and compulsory forms of rehabilitative therapy, would be sanctioned by the law or morality (for a more detailed discussion of this issue, see Baccarini & Malatesti, 2017).

To recapitulate our discussion, our conclusion is that the introduction of biomarker-based classification of antisocial behaviors should not be resisted on the basis of ethical objections concerning "biologization", such as stigma or negative self-image. However, our discussion leaves untouched several serious issues, and, thus, it should be appreciated that our conclusion is circumscribed. We describe these further problems in the following section.

Open issues

An important issue that needs to be addressed concerns the possibility that people in fact would stigmatize those who are diagnosed or classified based on biomarker information despite lacking normative foundations for these attitudes. Properly addressing the latter issue requires further investigation of how to devise public policies that narrow the potential gap between our normative argument and people's actual attitudes about the significance of biocognitive markers characterizing individuals with antisocial personality structures. We argued that biomarker-based classification of antisocial behavior does not warrant worries related to medicalization, stigmatization, and essentialism. The question remains how to use these theoretical insights to effectively shape public opinion. This is an important problem of great empirical and practical complexity. Thus, to set public policies regarding the treatment of antisocial behavior and communicating the relevant scientific and normative arguments to the public, further ethical discussions are needed. These discussions should be sensitive to the trade-offs between the reliability and the precision of the currently available science and its impact on the wellbeing and intrinsic rights of the relevant groups of people (Kitcher, 2001). We believe that further sociological and psychological investigation is needed before this implication can be addressed properly (Pickersgill, 2012).

Another set of issues that still need to be addressed relate to the empirical reliability of available science and its ethical implications. For instance, some have claimed that psychopathy is characterized by diminished experience of fear, which might be one of the factors influencing their imperviousness to aversive learning as well as the altered development of normal capacities underlying control and moral sense (Blair, Mitchell, & Blair, 2005; Glenn, Raine, & Laufer, 2011). If this is the case, then we might consider devising therapies that could restore normal experience of fear, especially if this would enable mitigation of antisocial tendencies correlated with psychopathy.

However, a prerequisite for thinking about this issue is to answer some empirical and ethical questions. First, the question is whether we have reliable skills and secure technology to produce treatments of this type (Harris, 2011; Persson & Savulescu, 2012). Second, we have to be confident in the precision of the empirical results and theories that are used to ground treatments and ethical policies. This point is nicely illustrated with the case of psychopathy. Despite the common opinion that psychopaths have impairments in *subjectively experiencing* fear, there is no conclusive evidence showing this (Hoppenbrouwers et al., 2016). Instead, the deficits seem to involve mechanisms underlying responses to threatening stimuli (Brazil et al., 2018; Koenigs & Newman, 2013). And, third, even if the first two conditions are satisfied we still have to answer the ethical question whether it would be ethically correct to use such treatments. Remaining with our current example, if somebody does not experience fear, or experiences it to a lesser degree, then undergoing therapy for remedying this abnormality would likely involve inducing unpleasant and aversive sensations, among other things. Thus, we would have to decide whether it is ethically permissible to use such therapies even if they were technologically and practically feasible. These are the questions that in the future research will need to be addressed more thoroughly (Harris, 2011).

Finally, there are important open ethical questions concerning how to deliver the treatment that biomarker-based classifications might afford. In fact, this type of classification could enable us to intervene with biological means in the moral capacities of the agent (Glannon, 2014; Persson & Savulescu, 2012). Whether and how we should intervene on these human capacities is a debated issue amongst ethicists (Baccarini & Malatesti 2017, 2017; Douglas, 2014; Harris, 2011; Hübner & White, 2016; Pugh & Douglas, 2016; Shaw, 2013).

Conclusion

There are empirical and theoretical reasons for introducing a biomarker-based classification for adult

antisocial individuals. It can be concluded that biomarker-based classification has the potential to provide new avenues and opportunities for devising effective treatments.

We have argued that two principal ethical worries about this type of classifications can be defused. First, given the limited knowledge of biomarkers' predictive value and the structure of our judiciary systems, bioprediction of criminal behavior should not be the most pressing source of ethical concern. Second, we have investigated whether biocognitive classifications of antisocial behavior offer rational grounds for stigma or negative self-evaluation. We have denied the existence of these grounds, by showing that these classifications do not imply essentialism, immutability, and determinism.

Our conclusions, however, cannot be seen to amount to unqualified and general defense of adopting biomarker-based classification of antisocial disorders. We have, in fact, signaled several interrelated empirical and ethical issues that need clarification and further investigation. However, we also think that we have given some reasons for optimism by showing that, *per se*, the adoption of a biomarker-based classification does not have the ethically problematic consequences that some have envisaged.

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